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Report to the Chairman, Subcommittee on Oversight and Investigations, Committee on Energy and Commerce House of Representatives

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BIOTECHNOLOGY

Analysis of Federally Funded Research

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Resources, Community, and
Economic Development Division

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The Honorable John D. Dingell
Chairman, Subcommittee on Oversight
and Investigations
Committee on Energy and Commerce
House of Representatives

Dear Mr. Chairman:

As requested in your December 9, 1985, letter and subsequent discussions with your office, this report verifies and analyzes some of the data collected by your Subcommittee as part of its inquiry into the federal government's role in biotechnology. It also provides information on how various agencies define biotechnology research and how to view biotechnology risk assessment research.

In August 1984 and again in April 1985, the Subcommittee surveyed 11 federal agencies about the nature of all biotechnology-related research they support. You asked specifically that we develop biotechnology research activity profiles for five of the agencies: the Department of Agriculture (USDA), the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the National Science Foundation (NSF). Each profile includes estimates of the fiscal year 1985 level of support, in terms of dollars obligated and number of projects funded, for

- agencywide activity for the conduct of research and development,
- biotechnology-related research, and
- biotechnology risk assessment research.

The data for these estimates were compiled by contacting officials in agency budget offices and agency program offices, and from written responses to the Subcommittee's surveys.

A summary of information on biotechnology research funding and the number of projects supported by each agency is included in this letter. The detailed results of our data collection and verification are presented in appendixes II through VII. In the course of our work, we found wide differences in the way these agencies interpret "biotechnology" and "risk assessment" for the purposes of policy making. The issues relating to the definition of biotechnology research and to biotechnology risk assessment are discussed below.

Issues Related to Defining Biotechnology Research

Biotechnology is not a discrete subject but rather a new term for which there is no formal agreement on a definition. We found that each of the agencies we contacted defines the term differently. In fact, definitions vary so widely that the estimates of support for biotechnology research cannot be meaningfully compared. Congressional attempts to legislate or regulate in this area could be difficult without a clear understanding of the terms used.

Varying Definitions of Biotechnology

In the Federal Register notice issued December 31, 1984, biotechnology was defined by the White House Domestic Policy Council Working Group on Biotechnology as "the application of biological systems and organisms to technical and industrial processes." This definition was reported as the standard at EPA, FDA, and NSF. However, each agency has developed a working definition that is somewhat more precise in either its scope or purpose.

We found wide diversity in the working definitions not only between agencies but, in the case of USDA, between two research organizations in the same agency. For example, the narrowest working definition of biotechnology research was found at EPA. Its research activities, funded at $1.5 million, focus on evaluating scientific questions associated with the field applications of genetically engineered microorganisms. In contrast, NIH defines research related to biotechnology to encompass a much wider range of topics. It classifies biotechnology into two categories: (1) basic research directly related to the "new biotechnology" (funded at $639 million)— which includes gene manipulation, hybridoma/monoclonal antibody work, and several subjects dealing with natural and synthetic proteins and nucleic acids—and (2) science base research underlying the new biotechnology (funded at $1.21 billion)—which includes investigations into genetics, molecular and cell biology, and immunology. As broad as this latter category is, it is still narrower than the definition of biotechnology-related research used by NSF. Included in the NSF definition, beyond the topics in NIH's science base area, are a wide range of areas in chemistry; many engineering fields applicable to bioprocessing; parts of environmental biology; and other areas of biology, including bioelectronics, bioenergetics, and reproduction. NSF awarded $81.6 million for this work in fiscal year 1985.

In addition, since biotechnology is not a field of science but draws from biology, engineering, and other established fields, it is somewhat arbitrary to categorize work on this subject. As a consequence, biotechnology-related research is often not separately identified in an agency's

budget, but is intermingled with other activities. Therefore, it is difficult to estimate an agency's level of biotechnology research support. Because of this lack of a coherent definition and a corresponding data collection system, the estimates of biotechnology research funding shown in this report should not be aggregated across agencies; neither should comparisons be made of the relative size of agency biotechnology research budgets.

Because of the inconsistent interpretation of the term "biotechnology," the definitional issue could be a significant problem in the event that the Congress considers regulations in some areas of biotechnology. It may be useful, for the purpose of discussing possible regulatory approaches, to avoid the term "biotechnology" and instead use more specific terms such as "deliberate or accidental release of genetically engineered microorganisms."

Mission-Related Biotechnology Research

Another observation from our review is that the purposes for which federal agencies undertake biotechnology research vary. In other words, the differences in the agencies' interpretations of biotechnology research reflect the differences in their missions. We identified three different categories in which research activities could be classified, as follows:

1. Basic research into the science that underlies biotechnology: this is basic scientific investigation for understanding biological processes and phenomena. NIH and NSF are the main supporters of this kind of research. Results of fundamental biological research will often provide the basis for applied work that leads to new biotechnology, but the aim of the work remains knowledge. In many cases, the understanding obtained in basic research can provide information useful in understanding and assessing health and environmental risks, but this result is incidental rather than the purpose of the work.

2. Applied research and technology development, using the new techniques of biological research: this work is done to devise, apply, or improve products and processes. Examples at USDA include using monoclonal antibodies to improve plant nitrogen fixation rates or help protect livestock against disease, and using tissue and protoplast cultures to improve selectivity of herbicide chemicals. At FDA, monoclonal antibodies have been applied in developing new medical testing kits, and synthetic DNA has been used to detect the AIDS virus. Results of some of this research will be subject to the federal regulatory process. Even

when projects overlap into basic research because they are explicitly seeking an understanding of some biological process or phenomenon, the intent to use the result for some practical purpose identifies it as applied.

3. Research for regulation: these activities develop information for assessing the potential risks associated with new products and processes developed from applying biotechnology. In general, research is designed to aid agency officials in determining the risks of moving from experimentation in contained facilities to field testing and commercial use. The regulatory agencies we reviewed tend to undertake research to deal with their unique responsibilities. At EPA, for example, a study was funded on the survival and fate of genetically engineered microbes in insects feeding on plant leaves that had been sprayed with such microbes. This research class should be understood to include efforts to gather and use knowledge already obtained in basic and applied research for examining regulatory questions.

In addition to projects that fit any of these categories, some projects have been included in agency listings of biotechnology research simply because they used certain biotechnological techniques as tools for carrying out the research. However, if biotechnology is only used as a tool and is not intrinsic to the process or product, then it is somewhat confusing to classify the work as biotechnology research. Thus, a definition that focuses only on the use of biotechnology is not sufficient.

Issues Related to Biotechnology Risk Assessment Research

Risk assessment[1] is a process for systematically organizing and interpreting information about the health and/or environmental risks that may arise from an action, in this case from applying biotechnology. It identifies and characterizes risk sources; assesses exposure to them; analyzes the relationship between amount of exposure and extent of effect(s); and makes an overall estimate of risk, with a range of uncertainty.

Information learned from any research project might contribute to biotechnology risk assessment, but the contribution would not occur or be recognized until some application of the particular biotechnology process or product was proposed. We therefore classified risk-related

[1]The full definition of risk assessment is found in app. I. It is based on material from The Suitability and Applicability of Risk Assessment Methods for Environmental Applications of Biotechnology, V.T. Covello & J.R. Fiksel, eds., National Science Foundation (Aug. 1985).

research projects into two categories: (1) research involving one of the activities included in risk assessment, or developing methods or tools for it, as applied to the specific subject being addressed in the project and (2) research providing information to help understand the biological system involved in the project, which could contribute to risk assessment if a product were to be developed based on this biological system.

Research Directly Involved in Risk Assessment

While agency definitions of biotechnology differed too widely to allow quantitative comparisons of their support of biotechnology research, we were able to derive estimates of biotechnology risk assessment research that can be compared across agencies by applying a uniform definition. We examined research projects to see if they were either seeking answers to questions posed by risk assessment or were developing methods or tools to do so. Projects meeting this criterion were classified as "direct risk assessment."

Of the projects we examined, in general, only a small number could be classified as direct risk assessment. At USDA's Agricultural Research Service, we estimated that between 4 and 27 of about 150 intramural projects, and at NSF between 8 and 225 of 1,773 projects involved direct biotechnology risk assessment. At FDA, we found that, at most, 6 out of 30 projects (accounting for less than 4 percent of reported biotechnology expenditures) appeared to be directly involving biotechnology risk assessment. USDA's Cooperative State Research Service could provide descriptions for only about two-fifths of the biotechnology research spending reported. We found that, at most, 22 of an estimated 138 biotechnology projects in this portion of the Service's research were directly doing risk assessment. EPA was the exception; all 19 projects funded by that agency were performing risk assessment. (These included three conferences aimed at reviewing knowledge available from research supported by others.) Finally, because of inconsistencies in the way NIH data are developed, we did not examine information on which the determination could be made for the vast majority of projects at NIH.

We had anticipated that EPA and FDA would be most involved in direct biotechnology risk assessment, since such efforts appear central to their regulatory missions. This proved true for EPA, where all projects were directed toward assessing potential risks related to the release of genetically engineered microorganisms.

However, the FDA biotechnology research projects did not appear to conform to this expectation: few of them involved risk assessment. In our discussions with FDA officials, we were told that all of their research is aimed to serve their overall mission of assessing the risks of products they regulate. We might have seen how certain projects were risk-related, if we had been able to follow some examples of biotechnological product reviews through FDA's regulatory process. In the time available for this study, however, we were unable to examine this possibility.

A second reason why our examination did not identify all FDA biotechnology risk assessment research is that FDA primarily examines materials or devices on the basis of the type of product proposed, rather than on how it was made. A drug or vaccine could be tested in the same way whether it was produced by traditional methods or through the use of new biotechnology. If research to examine possible risks of products derived from biotechnology were done by nonbiotechnological methods, the experiments would not have been included among the biotechnology research projects FDA listed in response to this inquiry. FDA officials pointed out that, in fact, numerous medical test kits for laboratory use based on new biotechnologies had been examined using previously available approaches. These were instances where the risks of biotechnology products were being assessed without the use of biotechnological methods.

Research Providing Background Information for Risk Assessment

For any project not examining the risks of the product or process it was studying, the question was to determine whether, if the subject of the project were to be applied to a process or product, that project's results would then contribute information useful to risk assessment. The risk assessment study that we reviewed for our definition, which was focused on biotechnology involving the release of genetically engineered microorganisms, gave major emphasis to the usefulness for risk assessment of knowledge about the basic microorganism being used.[2] We regard basic knowledge about the biological process or technique involved as being of similar importance in any biotechnology. Looking at projects not already assessing current risks, we found that most of the projects from each agency for which we had descriptions did fit into this category, providing background knowledge useful for risk assessment.

We did not obtain official agency comments on this report. The views of responsible agency officials were obtained during our work and are

[2]Covello and Fiksel, pp. 15-17 and 35-36.

incorporated into the report where appropriate. As arranged with your office, unless you publicly release its contents earlier, we will not release this report further until 30 days after the date of this letter. At that time copies will be sent to the Secretary of Agriculture; the Administrator, Environmental Protection Agency; the Commissioner, Food and Drug Administration; and the Directors of the National Institutes of Health and the National Science Foundation. Copies will be made available to others upon request.

Sincerely yours,

J. Dexter Peach

J. Dexter Peach
Director

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Abbreviations

ARS	Agricultural Research Service
CDB	Center for Drugs and Biologics
CSRS	Cooperative State Research Service
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FY	fiscal year
GAO	General Accounting Office
NIEHS	National Institute of Environmental and Health Sciences
NIH	National Institutes of Health
NSF	National Science Foundation
OMB	Office of Management and Budget
R&D	research and development
USDA	Department of Agriculture

Objective, Scope, and Methodology

The objective of this review was to verify and analyze data on federal support for biotechnology research in fiscal year 1985. The Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, staff selected five federal agencies for us to review: the Department of Agriculture (USDA), the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the National Science Foundation (NSF). Because of differences in the way biotechnology is defined, we decided to report separately on USDA's two principal research organizations, the Agricultural Research Service (ARS) and the Cooperative State Research Service (CSRS), which together account for about 95 percent of USDA's reported biotechnology research expenditures.

For each agency, we were asked to report the dollars obligated and the number of projects funded for the following activities:

- Agencywide activity for the conduct of research and development.
- Biotechnology-related research.
- Biotechnology risk assessment research.

In addition, we were asked to analyze some related issues, including agency definitions of biotechnology. In the cases of ARS, NSF, and the majority of the institutes at NIH, agency program officers were able to determine the proportion of a research project engaged in biotechnology-related activities, and so we have verified and reported on the prorated amounts. (We did not attempt to verify the correctness of the proportions selected by the agency.) For the other agencies, where partial content was not accounted for, the data represent the total level of funding for projects identified as biotechnology-related. Where the data were available, we have indicated whether the research was conducted intramurally or extramurally.

Agencywide Research and Development

Data on the size of agency budgets for the conduct of research and development were obtained from the Office of Management and Budget (OMB). Where possible, the corresponding number of projects was obtained from agency budget offices. Estimates of each agency's biotechnology research expenditures and numbers of projects were reported by agency program or policy officials. Few of the agencies, however, could provide estimates on the level of funding or the number of projects in support of biotechnology risk assessment research. This was due largely to the uncertainty about the application of research results to risk assessment work. For this category, therefore, we derived

ar estimate on the basis of an examination of project descriptions supplied by the agencies.

Verifying Biotechnology Research Estimates Reported by the Agencies

To verify the data reported by the agencies on biotechnology-related research, we sought to confirm whether the data being reported were actually for biotechnology-related research. We recognize that agencies differed in their interpretion of what activities to include as biotechnology research. Therefore, we verified the agency estimates by comparing descriptions of research projects identified by them as biotechnology-related with the definition of biotechnology used at each agency. The projects we found not to fit the definitions were excluded because they did not explicitly indicate the involvement of one of the research techniques or research activities specified in either the definition of biotechnology-related research or risk assessment. However, some of the project descriptions were limited in detail. If the agencies had provided more detailed descriptions of the projects, they may well have indicated use of one of the specified methods or objectives. This is especially true of the abstracts examined for CSRS and FDA. It should be noted that this procedure would only detect errors on the part of the agencies that produced overestimates of their biotechnology research support. Because we relied on information provided by the agencies, we were not able to identify any biotechnology projects that the agencies failed to report to us. Because of this limitation on verification, as well as the differences in definition, the data we present should not be aggregated across agencies or compared between agencies.

Agency definitions of biotechnology were obtained from their responses to the Subcommittee surveys of August 1984 and April 1985. However, they lacked the specificity required to distinguish biotechnology related research from other research activities. Some of the agencies further distinguish their biotechnology-related research through the use of "biotechnology indicators" and "key words." Where these "working definitions" were available, we used them as the criteria for judging the project conformance.

For ARS, EPA, and FDA, we obtained a complete set of abstracts describing all of those projects identified by the agency as biotechnology-related. Because of the large number of projects involved for CSRS and NSF, we selected abstracts on the basis of a random sample. The sample size for each agency was selected to estimate the proportion of biotechnology projects and produce a sampling error of within approximately 10 percent of the actual proportion at the 95-percent confidence level. For NIH,

we obtained computer printouts from each institute listing all the biotechnology-related work being funded. However, because of the large number of projects and institutes involved, and variations across institutes in the manner in which data bases were developed, we did not verify the NIH estimates by comparing abstracts with definitions.

GAO Estimates of Biotechnology Risk Assessment Research

To determine how much of the biotechnology-related research was for the performance of risk assessment, we decided to use a uniform, well-accepted definition of risk assessment as the criterion. The definition we used was adopted from an August 1985 report by Vincent T. Covello (NSF) and Joseph R. Fiksel (Arthur D. Little, Inc.), entitled The Suitability and Applicability of Risk Assessment Methods for Environmental Applications of Biotechnology. The study was prepared for the Office of Science and Technology Policy and has been used by the Biotechnology Science Coordinating Committee. The definition of biotechnology risk assessment activities we used is as follows:

Assessment of risks associated with environmental applications of biotechnology. This process consists of:

- Identification of risk: designating its source, mechanism of action, and potential adverse consequences.
- Characterization of the risk source: describing types, amounts, timing, and probabilities of harmful events.
- Assessment of exposure: estimating intensity, frequency, and duration of exposure to risk agents.
- Assessment of dose-response: characterizing the relationship between the dose of risk agent received and the health or other consequences.
- Estimation of risk (integration of the above, including a range of uncertainty).

Further development of methods or tools to carry out the process of risk assessment of biotechnology applications. Procedures fall into the following categories:

- Human exposure and effects analysis.
- Ecosystem structural and functional analysis.
- Environmental fate and transport analysis.
- Ecological consequences assessment.
- Evaluation of microorganism properties.
- Controlled testing and monitoring.

In the cases of EPA and FDA, our estimates of the number of biotechnology projects involved directly in risk assessment are based on an examination of all of those project descriptions supplied by the agencies and verified as biotechnology. For ARS, CSRS, and NSF, our estimates were drawn from the results of applying the definition to a random sample of verified biotechnology projects. Because we did not verify NIH data on biotechnology research support, our discussion of risk assessment at NIH is based on a limited review. We examined only those projects funded by the National Institute of Environmental Health Sciences (NIEHS), the institute reported by NIH officials to be most likely to investigate some of the questions listed above.

Agricultural Research Service

Agencywide Research and Development

ARS is the primary scientific research agency within USDA. Its mission includes developing new knowledge and technology to improve agricultural productivity, and providing scientific support for various regulatory agencies at USDA. It conducts research in five general areas: soil and water conservation, plant and animal productivity, commodity conversion and delivery, human nutrition, and integration of agricultural systems.

As shown in table II.1, in fiscal year 1985, ARS programs obligated about $470 million for the conduct of research, accounting for about half of USDA's total research budget of $941 million. Over half of the ARS dollars were for the performance of basic research, 41 percent for applied research, and 6 percent for development. ARS research funds supported about 2,300 projects, the bulk of which were done intramurally at numerous field locations.

Table II.1: Profile of ARS Research Activity, FY 1985

	Total conduct of R&D[a]	Biotechnology research[b]	Biotechnology risk assessment
Total:			
Obligations (millions)	$469.7	$24.5	(c)
Number of projects	2,300	(c)	(c)
Intramural:			
Obligations (millions)	$443.5	$23.0	(c)
Number of projects	1,775	150	4 to 27[d]
Extramural:			
Obligations (millions)	$26.2	$1.5	(c)
Number of projects	525	(c)	(c)

[a]Total obligations were obtained from unpublished materials prepared by OMB for Special Analyses, Budget of the United States Government, 1987, Special Analysis K (dated Jan. 16, 1986). The distribution of total dollars between intramural and extramural research is based on shares calculated from estimated FY 1985 data in NSF, Federal Funds for Research and Development, Fiscal Years 1984, 1985, and 1986, volume 34, table C-8. We estimated the number of projects on the basis of average project cost data provided by ARS.

[b]GAO dollar estimates were derived by adjusting ARS data by the percentage of actual biotechnology research found through the verification process. We estimated the number of intramural biotechnology projects assuming an average project cost of $150,000.

[c]Not available.

[d]GAO estimate based on an examination of a sample of 39 ARS intramural biotechnology research projects as of March 1986.

Biotechnology Definition Used by ARS

In a February 1985 internal report, ARS recognized the definitional problem encountered when trying to distinguish biotechnology research from other fields of research. The agency referred to biotechnology as a "rather dimensionless and somewhat ambiguous term." In order to have a consistent measure for its data collection, and to help all parties understand the term, ARS defined biotechnology research as:

"projects [which] used techniques such as gene cloning in microorganisms, nucleic acid hybridization, biological and biochemical synthesis of nucleic acids and proteins, use of monoclonal antibodies, affinity column separation of antigens, use of immobilized enzymes and cells, protoplast fusion, regeneration of plants from tissue culture, transfer of embryos, gene mapping, and synthesis of peptide neurohormones."

To further help its scientists and program staff identify such research, a set of "biotechnology indicators" was developed. It consists of four categories of research activities: genes, membranes, mediators, and bioregulation/bioconversion.

Biotechnology Research Activity

USDA's Office of Budget and Program Analysis reported that in fiscal year 1985, ARS obligated $26.5 million for biotechnology research, an increase of 72 percent over fiscal year 1984 funding. Relative to ARS' total budget for the conduct of research and development, the biotechnology component accounted for 5.6 percent. The allocation of the estimated biotechnology spending among ARS program activities was $10.2 million for research on plant productivity (with $2 million to the Albany, Calif., Gene Expression Center), $8.8 million for reseach on animal productivity, $7.3 million for research on commodity conversion and delivery, and $200,000 for soil and water conservation research. As a result of our verification process, and as explained below, ARS' total biotechnology reseach dollars were adjusted to $24.5 million.

In developing its data base, ARS' Program Planning and Review staff recognized that many projects use a biotechnological tool for only a small part of the work. To obtain a more accurate estimate of biotechnology research, determinations were made by agency staff as to the proportion of each project that was employing biotechnology. On the basis of project descriptions prepared by agency scientists, estimates to the nearest 10 percent were assigned to indicate the share of the research employing biotechnology.

The Director of Budget and Program Management at ARS estimated that ARS' total biotechnology dollars contributed to between 160 and 180 research projects in fiscal year 1985.

In March 1986, we obtained a computer printout showing all ongoing ARS intramural biotechnology research activity. Extramural work, estimated at 5.6 percent of the biotechnology research expenditures, is not recorded in the ARS computer system and therefore was not verified. Because the ARS data base is continually updated, we could not possibly match the fiscal year 1985 budget estimates of biotechnology research funding with the documentation received from the computer system in March 1986. Because of the timing discrepancy, we have derived approximate figures for ARS' fiscal year 1985 biotechnology research by verifying the March 1986 sample and adjusting ARS' fiscal year 1985 estimates accordingly.

The documentation obtained in March 1986 consisted of abstracts of 155 active intramural research projects whose biotechnology components totaled $23.3 million. We verified ARS' estimate of the biotechnology content of this listing by comparing the description of each project's objectives and approach with the biotechnology definition described above. Our examination of the March 1986 data revealed that $21.4 million of the $23.3 million conformed to the agency's definition. Using this proportion, we estimate that $23 million (representing about 150 projects) of the $25 million reported by ARS for fiscal year 1985 was spent intramurally on biotechnology research. By adding in $1.5 million for extramural research projects, we derive a total of $24.5 million.

Biotechnology Risk Assessment Research

We examined a randomly chosen sample of 39 of the March 1986 ARS intramural biotechnology research projects to determine whether projects conducted by the agency were aimed at assessing the risks of biotechnology. We found that about 10 percent of the biotechnology projects in our sample were for the performance of risk assessment.[1] Applying this result, we would expect that between 4 and 27 of the estimated 150 intramural projects conducted in fiscal year 1985 were directly assessing risks associated with biotechnology. About 87 percent of the sample projects could provide background knowledge useful in doing risk assessments, and only a small fraction—less than 3 percent of

[1]Our sample result indicates that between 3 and 20 of 113 projects being conducted in March 1986 were biotechnology risk assessment research.

the projects—was found to totally lack risk assessment-related research.

GAO Observations

We found that ARS' definition of biotechnology and the descriptions of its projects fit largely into two classes of activity:

- applied research and technology development: work done to seek and test ways of controlling or adapting the biological materials and processes for commercial use relevant to agriculture, and to a lesser extent,
- basic science (mostly molecular biology): work done to obtain knowledge about biological materials and processes related to agriculture.

Thus, our examination of the research abstracts and supporting material on ARS' program objectives indicates that the emphasis throughout is indeed on using biotechnology, and to a lesser extent on advancing knowledge of the underlying science. None of the ARS literature we examined took any note of possible questions about risks that may accompany such development and use. As discussed above, we found very little work oriented toward examining or clarifying such questions. It is possible that additional work related to assessing risks of biotechnologies is supported by other parts of USDA, such as the Animal and Plant Health Inspection Service. Since we only examined the research programs of two services in USDA, we would not have identified such work.

Cooperative State Research Service

Agencywide Research and Development

CSRS is USDA's principal liaison to the state university system for the conduct of agricultural research. As authorized by a number of statutes, it administers grants and payments to state agricultural experiment stations and other eligible institutions to supplement state and local funding. In addition, CSRS assists in agricultural research program planning and coordination between state institutions, USDA, and the agricultural industry. Research programs are submitted for approval by CSRS and are evaluated periodically by CSRS staff.

As shown in table III.1, in fiscal year 1985 CSRS obligated about $284 million in research support, divided almost equally between basic and applied research activities. This represented about 30 percent of USDA's budget for the conduct of research and development. Except for federal administrative expenses, less than 4 percent of the total, CSRS funds went entirely for the support of extramural program activities.

Over half of the CSRS research budget in fiscal year 1985 was for payments under the Hatch Act. Under the Act's program, funds are allocated on a formula basis to agricultural experiment stations of the land grant college system "for research to promote a sound and prosperous agriculture and rural life." Another $46 million, or 16 percent of CSRS' research obligations, was for the Competitive Research Grants program. Under this program, scientists compete for funding to support basic research critical to food production and human nutrition. Other programs included Special Research Grants, payments to "1890 Colleges" and Tuskegee University, and Cooperative Forestry Research.

Table III.1: Profile of CSRS Research Activity, FY 1985

	Total conduct of R&D[a]	Biotechnology research[b]	Biotechnology risk assessment
Total:			
Obligations (millions)	$284.3	$48.4	(c)
Number of projects	12,250	750	(c)
Intramural:			
Obligations (millions)	$10.2	$0	0
Number of projects	0	0	0
Extramural:			
Obligations (millions)	$274.1	$48.4	(c)
Number of projects	12,250	750	(c)

[a]Total obligations were obtained from unpublished materials prepared by OMB for Special Analyses, Budget of the United States Government, 1987, Special Analysis K (dated Jan. 16, 1986). The distribution of total dollars between intramural and extramural research is based on shares calculated from estimated FY 1985 data in NSF, Federal Funds for Research and Development, Fiscal Years 1984, 1985, and 1986, volume 34, table C-8. Intramural funds cover costs associated with the administration of extramural programs. We estimated the number of projects on the basis of average project cost calculations.

[b]Obligations estimated by USDA's Office of Budget and Program analysis. BECAUSE OF THE LACK OF DOCUMENTATION ON HOW CSRS IDENTIFIED BIOTECHNOLOGY PROJECTS, WE COULD ONLY EXAMINE 153 PROJECTS, COVERING $19.2 MILLION. THE RESULTS OF OUR SAMPLE INDICATED THAT BETWEEN 109 AND 148 OF THE PROJECTS WERE BIOTECHNOLOGY RELATED.

[c]Owing to the lack of documentation as noted above, we could not estimate biotechnology risk assessment research activity for all of CSRS. However, sampling results indicate that, at most, 22 of an estimated 138 biotechnology projects in the portion of CSRS research we examined were doing risk assessment.

Definition of Biotechnology Used by CSRS

CSRS uses a definition of biotechnology research developed by the Division of Agriculture's Committee on Biotechnology of the National Association of State Universities and Land-Grant Colleges. The Committee membership includes individuals with administrative responsibility for agricultural research and education programs in land grant institutions. In a progress report issued November 1983, the Committee noted that agriculture has been using living organisms and their components in industrial processes for over 80 years. However, as a research activity, it describes "biotechnological research" as utilizing an array of new techniques that are based on molecular and cellular genetics and developmental biology. Furthermore,

"'Biotechnology' refers to the improved or modified organism, microbe, plant or animal, and 'new research techniques' or 'technology' refers to contemporary 'tools' available to scientists for the purpose of biotechnology development."

To obtain information on the biotechnology research funded by CSRS in fiscal year 1984, for a previous report, we and the association jointly

developed and distributed a questionnaire to all state agricultural experiment stations. (See GAO/RCED-86-39BR for survey results.) The definition of biotechnology research used in the survey was

"... the process of in vitro alteration of genetic material for the purpose of creating new gene combinations or modifications. [It] is limited to research involving the following biotechnology research techniques:

Direct manipulation of the genome using recombinant DNA, chemical synthesis of nucleic acids, and/or site-directed mutagenesis. (These techniques are often known as genetic engineering.)

Direct manipulation of cells (altering genetic information) using microinjection, transfection, transformation, embryo transfer, and/or cell and protoplast culture and fusion (i.e., using other biotechnology research techniques)."

Our interviews with CSRS' Principal Scientist confirmed that the budget data presented in table III.1 correspond to this definition of biotechnology research.

Biotechnology Research Activity

The amount of biotechnology work supported by CSRS is difficult to measure. Individual programs within CSRS differ not only by objective but also by having different funding mechanisms. Currently, there is no centralized data management system to track all funding in this area.

CSDA's Office of Budget and Program Analysis reported that CSRS obligated a total of $48.4 million toward biotechnology research in fiscal year 1985, including $30 million in Competitive Research Grants; $12.2 million as payments under the Hatch Act; and $6.2 million in Special Research Grants, Forestry Competitive Grants, and others. We estimated that these funds supported, in whole or in part, about 750 extramural projects.

The fiscal year 1985 level of support for biotechnology was more than double that for the previous year. This was the result of a congressional appropriation that increased the Competitive Grants program by $20 million that was specifically targeted for agricultural biotechnology. CSRS established six program areas for funding grant proposals with the new biotechnology funds: plant growth and development, plant molecular biology, responses to biological stress, responses to environmental stress, animal growth and development, and animal molecular biology. In fiscal year 1985, this biotechnology program received 890 proposals

requesting $257.8 million; 166 grants were awarded totaling $19.2 million.

We were able to obtain abstracts of 153 research projects funded under the Competitive Grants biotechnology program area, from which a sample of 20 projects was examined for verification. On the basis of the sample results, we estimate that between 109 and 148 of that program's 153 projects fit the stated definition of biotechnology research. CSRS lacks a data management system capable of identifying projects in the biotechnology area of agricultural science. Therefore, it was not possible for us to obtain the materials necessary to verify the remaining $29.2 million in fiscal year 1985 biotechnology research support estimated by CSRS. Development of a national biotechnology data base covering CSRS, ARS, and agricultural experiment stations is now underway at CSRS.

Biotechnology Risk Assessment Research

We examined all of the projects that met the biotechnology definition from our earlier sample of CSRS projects to determine the extent to which they would contribute to risk assessment for possible applications of biotechnology. We found that none of the projects in the sample performed the work that would constitute risk assessment. However, we found that all of the projects would contribute some information that could be useful background knowledge for risk assessment of technologies that might be developed based on the research. These sample results indicate that, at most, 22 of an estimated 138 biotechnology projects in this particular CSRS program are likely to be aimed directly at risk assessment, but almost all could contribute background knowledge for risk assessment activities.

GAO Observations

Comparison of the definition of biotechnology used by CSRS with that used by ARS indicates that the ARS definition is significantly broader. In particular, ARS included in its definition two categories of biological subjects not included by CSRS—membranes and mediators. Also, another category called bioregulation/bioconversion by ARS is only partly covered by CSRS' definition. By and large, CSRS biotechnology program projects appeared to be more focused in the genetics area than those of ARS. In fact, on reexamination of ARS' list of biotechnology projects, we found that only about 60 percent of them fit into categories included by CSRS. However, the CSRS definition is still broader than that used by EPA, which focused largely on genetically engineered microorganisms, since CSRS still included work dealing with insects and crop plants and animals, as well as microorganisms.

Environmental Protection Agency

Agencywide Research and Development

EPA views itself primarily as a regulatory agency—not a research and development agency. Nonetheless, research programs accounted for almost one-quarter of the agency's operating budget in fiscal year 1985. Research and development in air, energy, hazardous waste, water, and other areas are designed to provide the scientific basis for regulatory activities.

As shown in table IV.1, in fiscal year 1985, EPA's budget for the conduct of research and development was approximately $320 million. About $125 million supported research conducted intramurally, either at headquarters or in 14 major laboratories and various field locations. The balance financed research and development through contracts, grants, and interagency agreements. The distribution of research dollars by activity was: 12 percent for basic, 55 percent for applied, and 33 percent for development.

Table IV.1: Profile of EPA Research Activity, FY 1985

	Total conduct of R&D[a]	Biotechnology research[b]	Biotechnology risk assessment[c]
Total:			
Obligations (millions)	$320.4	$1.5	$1.5
Number of projects	(d)	19	19
Intramural:			
Obligations (millions)	$124.7	$0.4	$0.4
Number of projects	(d)	7	7
Extramural:			
Obligations (millions)	$195.7	$1.1	$1.1
Number of projects	(d)	12	12

[a]Total obligations were reported in OMB Special Analyses, Budget of the United States Government, 1987, Special Analysis K (Feb. 1986). The distribution of total dollars between intramural and extramural research is based on shares calculated from estimated FY 1985 data in NSF, Federal Funds for Research and Development, Fiscal Years 1984, 1985, and 1986, volume 34, table C-8. Intramural funds cover costs associated with the administration of intramural and extramural programs as well as actual intramural performance.

[b]GAO estimates based on verification of data provided by EPA's Office of Research and Development.

[c]GAO estimates based on an examination of EPA's biotechnology research documentation.

[d]Not available.

Definition of Biotechnology Used by EPA

In a letter dated March 26, 1985, EPA responded to a request from the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, for information on the agency's biotechnology research program. In describing how it views work in this area, EPA wrote that

"Biotechnology is generally defined as the use of living organisms to yield products and can be traced to the early uses of microbes in baking, fermenting, and animal or crop husbandry. However, from the EPA's regulatory perspective, biotechnology is limited to the commercial application of molecular biology and genetics techniques resulting in the modification of industrial products and processes."

Since that date, EPA appears to have narrowed its definition of the term further to focus on one particular area of the "new biotechnology." The data on biotechnology funding presented in table IV.1 is based on the following definition provided by the Office of Research and Development in March 1986:

"We are defining biotechnology as the application of biological organisms to technical and industrial processes. It involves the use of 'novel' microbes which have been altered or manipulated by humans through techniques of genetic engineering."

Biotechnology Research Activity

EPA established a formal biotechnology program in fiscal year 1985. As reported by the Office of Research and Development, funding for biotechnology projects in fiscal year 1985 totaled $1.5 million, of which $0.4 million was conducted at intramural laboratories and $1.1 million was in the form of grants and contracts. The intramural research on biotechnology was conducted primarily at four EPA labs in Oregon, North Carolina, Florida, and Ohio. The majority of the extramural work was done by universities.

The dollars cited above supported a total of 19 research projects. To verify the data, we examined abstracts of each of these projects and found that they all were consistent with the definition of biotechnology used by the agency.

In a letter to the Subcommittee dated June 14, 1985, EPA described the overall purpose and scope of its research efforts in biotechnology as providing a basis for estimating the impact of biotechnology products on the environment and public health. To accomplish this, the research program focuses on the examination of methods and protocols to detect

potential problems that may result from application of specific products. The program has three components: health effects, environmental effects, and engineering.

Biotechnology Risk Assessment Research

In letters to the Subcommittee, EPA has noted that it conducts research projects specifically aimed at evaluating risks associated with biotechnology. Other research activities are intended to provide information that will

> "broaden [the agency's] knowledge concerning organisms that may be released into the environment and will also provide the background knowledge needed in health effects studies and in the development of predictive models."

Applying the description of risk assessment research discussed in appendix I, we found that all of the EPA biotechnology research described for the 19 projects and $1.5 million noted above was contributing directly to assessing the risks of biotechnology. Within the definition of risk assessment, every project was contributing to one or more of the "method development" areas, with all except the sponsoring of three scientific conferences focusing on the environmental fate and transport of genetically engineered microbes, and a majority also involving controlled testing and monitoring work.

GAO Observations

EPA's biotechnology research is focused on assessing the risks of the new technology, particularly on questions about genetically engineered microorganisms. In this context, the acting director of the Toxics and Pesticides Division (which performs research on biotechnology and microbial pest control agents), Office of Environmental Processes and Effects Research, explained that risk assessment at EPA is viewed as a three-stage process. As applied to genetically engineered microorganisms, the first element is to determine the biological hazard, that is, what are the effects of the organism on its environment? The second element is to determine the level of exposure to the organism for the environment and humans. The final step is to integrate both sets of information to derive an estimate of overall risk. This would include an indication of the degree of uncertainty (statistical probability) surrounding the risk assessment. This description of the risk assessment process corresponds quite closely to the one we have used.

Food and Drug Administration

Agencywide Research and Development

FDA, an agency of the Department of Health and Human Services, conducts basic and applied research in support of its regulatory and enforcement responsibilities. Its mission is to protect the public health against hazardous food, drugs, biologics (such as hormones, blood components, and vaccines), cosmetics, medical devices, and radiological products. Through product approvals and industry compliance and enforcement activities, FDA seeks to ensure the safety and efficacy of the products it regulates.

As shown in table V.1, in fiscal year 1985, obligations for research relevant to these activities were estimated at about $82 million. These funds accounted for about 20 percent of FDA's total budget obligations of about $419 million. Nearly all of its research activities are conducted intramurally within its five centers: the Center for Food Safety and Applied Nutrition, Center for Veterinary Medicine, Center for Drugs and Biologics, Center for Devices and Radiological Health, and the National Center for Toxicological Research.

Table V.1: Profile of FDA Research Activity, FY 1985

	Total conduct of R&D[a]	Biotechnology research[b]	Biotechnology risk assessment
Total:			
Obligations (millions)	$82.0	$2.6	(c)
Number of projects	(d)	17	(c)
Intramural:			
Obligations (millions)	$73.9	$2.6	(c)
Number of projects	(d)	17	(c)
Extramural:			
Obligations (millions)	$8.1	0	0
Number of projects	(d)	0	0

[a]Total obligations were reported in OMB Special Analyses, Budget of the United States Government, 1987, Special Analysis K (Feb. 1986). The distribution of total dollars between intramural and extramural research is based on shares calculated from estimated fiscal year 1985 data in NSF, Federal Funds for Research and Development, Fiscal Years 1984, 1985, and 1986, volume 34, table C-8.

[b]GAO estimates derived by adjusting FDA data through the verification process.

[c]Because of difficulties with prior application of the risk assessment definition to FDA work, no data are presented here. See text for details.

[d]Not available.

Definition of Biotechnology Used by FDA

Given its regulatory context, FDA views biotechnology as processes that can be used to manufacture the products subject to its review. Products derived from biotechnology range from those made with old biotechnologies, such as cheese, antibiotics, yogurt, and beer to those resulting from new biotechnologies, such as diagnostic devices using monoclonal antibodies and new drugs and biologics made with recombinant DNA technologies.

FDA uses the definition of biotechnology established by the Working Group on Biotechnology of the Domestic Policy Council. As reported to the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce,

"Biotechnology is the application of biological systems and organisms to technical and industrial processes. The technologies employed in this area include: classic genetic selection and/or breeding for purposes such as developing baker's yeast, conventional fermentation, and vaccine development; the direct in vitro modification of genetic material, e.g., recombinant DNA, or gene splicing, and other novel techniques for modifying genetic material of living organisms, e.g., cell fusion, and hybridoma technology, etc."

Biotechnology Research Activity

FDA documentation shows biotechnology research expenditures to be about $3.4 million for fiscal year 1985 although, as explained below, we adjusted this figure to $2.6 million. As in most of the other federal agencies, FDA has no designated facilities or comprehensive research programs specifically aimed at biotechnology. Scientists in four out of five of the agency's centers were reported to be involved in research related to the development and use of new biotechnological products, with the Center for Drugs and Biologics (CDB) conducting the bulk of the research.

In a letter to the Subcommittee dated October 10, 1985, FDA explained that "although all areas of research in CDB have the potential for biotechnology involvement, those projects directly related to [recombinant DNA and monoclonal antibody] techniques number approximately 24 at an annual (FY 1985) expenditure of $2.9 million."

We were subsequently provided descriptions of the $2.9 million of fiscal year 1985 CDB work listed as 14 (not 24) separate projects. The descriptions were, in many cases, quite brief, some barely more than one line of text. We were able to confirm that 11 of the 14, accounting for $2.4 million of the $2.9 million reported, fit the FDA definition of biotechnology.

For three projects with shorter descriptions there was not sufficient information to verify conformity with the definition.

In addition, FDA's Office of Operations Coordination provided descriptions of 16 projects, representing $486,915 in biotechnology expenditures, for three other centers and the Office of Regulatory Affairs. The largest part of this work was at the Center for Food Safety and Applied Nutrition, where four of six projects, accounting for $249,800, could be verified as fitting the FDA biotechnology definition. The one project reported at the Center for Devices and Radiological Health did not match the agency definition, and only two of the four small projects at the National Center for Toxicological Research did fit the stated definition. Finally, none of the five projects listed in the Office of Regulatory Affairs matched the definition.

Overall, for all FDA components reporting, 30 projects spending $3.4 million were cited as biotechnology projects; we found 17 fit the definition, which accounted for $2.6 million. It is our impression that the majority of the funds not covered in the biotechnology definition, the $520,000 represented by the three excluded CDB projects, would fit if they were described in more detail than the statements we were given. An FDA official acknowledged this shortage of information and indicated that had CDB provided more information, we would have found that more of these projects fit the definition. Most of the other 10 excluded projects, on the other hand, may have been reported under various other criteria, rather than those specified in the FDA definition of biotechnology; but they total only $231,115, representing less than 7 percent of the entire FDA biotechnology research estimate.

Biotechnology Risk Assessment Research

FDA's strategies for evaluating the safety of "biotechnological" or "genetically engineered" products are similar to those evaluating the safety of conventionally produced products. Although much information has been generated for conventionally manufactured products, according to FDA, some additional work might be required to do risk assessment of certain new products or techniques arising from new biotechnology, with particular emphasis on questions about the survival and the environmental effects of genetically engineered organisms. However, we found that only 1 of the 30 projects provided by FDA was oriented directly to assessing risks that might arise from biotechnology-derived products; FDA noted that biotechnology as used in that project was a tool for assessing chemical risks. That project, jointly sponsored with two other federal agencies, was funded at only $33,790 and did not

actually fit as a biotechnology project under FDA's definition. We did find that all of FDA's biotechnology projects were providing background information that would be of use in risk assessment.

If the five projects dealing with analytic methods and materials that were cited at the agency's Office of Regulatory Affairs were specifically aimed for use on biotechnological products or processes, perhaps they should also be counted as biotechnology risk assessment. Even if these projects are included, however, this would increase the estimate of expenditures on biotechnology research that is directly risk assessment to a total of about $100,000.

This finding, that less than 4 percent of FDA's biotechnology research expenditures could be considered risk assessment, points to a problem with our application of the risk assessment definition. In all cases, we have taken risk assessment to mean assessing the risks of the product or process that is the subject of the research. While this approach appears satisfatory in most cases, it may not take sufficient account of long-established risk assessment strategies in the agency. We suggest this may be true because, if an agency has been regulating a type of product for some time, it could recognize complex or indirect pathways in which risks might possibly arise, and it would then appropriately undertake research to investigate these possibilities, so as to assess them as risk sources. However, without an understanding of the history leading to this area of research, we probably would not recognize it as part of the agency's risk assessment activity because of its distant or indirect relationship to the regulatory matter in question.

It is this poor fit between the narrow application of the definition of risk assessment and the approach to risk assessment research at FDA that may explain why we found little direct biotechnology risk assessment research at FDA. Agency officials have pointed out that much of risk assessment research is generic, that is, not specifically biotechnology but relevant to it.

GAO Observations

FDA officials have repeatedly stated that in its regulatory activities, FDA focuses first on the type of product in question, rather than on how it was made. This would mean that the agency would pursue research questions, including research needed to assess risks on such subjects as a class of foods, drugs, or vaccines, for example. Research projects would quite often bear on all products or substances in the class, whether they were made by traditional or by new biotechnological

approaches. This would mean that research could bear on products made using new biotechnologies, whether or not the research itself involved biotechnology. For this reason, much research done by FDA might be relevant to new biotechnology products although it was not classified as biotechnology research and therefore not cited in FDA's response to our inquiry. Similarly, risk assessment research need not necessarily involve the same new biotechnological techniques that were used to make the product being assessed.

In both of these kinds of situations, research relevant to products of new biotechnologies (and the assessment of risks arising from them) could have been excluded from the agency's inventory of biotechnology research, even though the research might have played a significant role in FDA's regulatory consideration of products made using new biotechnologies. Judging the extent to which this may have occured would require in-depth examination of the content of a substantial part of FDA's research work and was beyond the scope of this report.

National Institutes of Health

Agencywide Research and Development

NIH, an agency of the Department of Health and Human Services, is the government's principal biomedical research agency. It conducts research in its own laboratories; supports the research of scientists in universities, medical schools, hospitals, and research institutions; helps train research investigators; and supports biomedical communication. NIH is composed of 12 separate institutes, a library, a clinical center, and other research resources.

As shown in table VI.1, in fiscal year 1985 NIH obligated about $4.8 billion for the conduct of research and development, making it by far the largest nonmilitary research agency in the federal government. These funds support about 18,000 project grants, 523 research centers, and 9,100 research trainees annually. The emphasis at NIH is on the conduct of basic research. About 63 percent of the agency's obligations for research and development activities in fiscal year 1985 was in the area of basic research, while about 29 percent supported applied research and 8 percent was for development.

Table VI.1: Profile of NIH Research Activity, FY 1985

	Total conduct of R&D[a]	Biotechnology research[b]	Biotechnology risk assessment
Total:			
Obligations (millions)	$4,824.4	$1,849.5	(c)
Number of projects	30,000	(d)	(c)
Intramural:			
Obligations (millions)	$919.3	$203.4	(c)
Number of projects	(d)	(d)	(c)
Extramural:			
Obligations (millions)	$3,905.1	$1,646.1	(c)
Number of projects	(d)	(d)	(c)

[a]Total obligations were reported in OMB Special Analyses, Budget of the United States Government, 1987, Special Analysis K (Feb. 1986). The distribution of total dollars between intramural and extramural is based on shares calculated from estimated FY 1985 data in NSF, Federal Funds for Research and Development, Fiscal Years 1984, 1985, and 1986, volume 34, table C-8. Intramural funds cover costs associated with the administration of intramural and extramural programs as well as actual intramural performance. The number of projects was reported by NIH.

[b]Dollar figures provided by NIH's Division of Financial Management but NOT VERIFIED BY GAO. The distribution of total dollars between intramural and extramural research is based on shares calculated from estimated FY 1985 data in NIH, Report on Biotechnology (Feb. 1985), p. 11. Extramural funds include research training expenditures.

[c]GAO did not estimate biotechnology risk assessment research activity for all of NIH. However, the results of our examination of NIEHS projects for risk assessment is discussed in the text.

[d]Not available.

Definition of Biotechnology Used by NIH

In a letter to the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, dated September 11, 1984, NIH described its definition of biotechnology as one which "takes into consideration the methodologies that are developed for the primary purpose of conducting basic research and the concepts that arise from this research." It accepts the definition developed by the Domestic Policy Council Working Group on Biotechnology, as follows:

"Biotechnology is the application of biological systems and organisms to technical and industrial processes. The technologies employed in this area include: classical genetic selection and/or breeding for purposes such as developing baker's yeast, conventional fermentation, and vaccine development; the direct in vitro modification of genetic material, e.g., recombinant DNA, or gene splicing, and other novel techniques for modifying genetic material of living organisms, e.g., cell fusion, and hybridoma technology, etc."

NIH support related to the development of the new biotechnology is characterized into two broad catagories: basic research directly related to biotechnology, and a larger science base underlying biotechnology. The following definitions are used to identify these categories:

- Basic research directly related to the new biotechnology includes manipulation of the genome, cloning of DNA, natural protein production by organisms; chemical synthesis of DNA and protein; use of special techniques to isolate, detect, and characterize DNA; creation of hybridomas and production of monoclonal antibodies; and computer methods used to analyze DNA and protein sequences, and to design new biopolymers.
- Science base research underlying the new biotechnology includes investigations into genetics, molecular and cell biology, and immunology.

Biotechnology Research Activity

Data on the allocation of resources to biotechnology was obtained from NIH's Division of Financial Management. For fiscal year 1985 NIH reported total support for basic research and research training related to biotechnology at about $1.8 billion, or 38 percent of the agency's entire budget for the conduct of research and development. About 84 percent of these funds supported extramural projects, while 11 percent was for intramural research and 5 percent for training.

NIH funding was split about $639 million for basic research directly related to the new biotechnology and about $1,210 million to develop the broader science base underlying the new biotechnology. Within the former category, the leading institutes were the National Cancer Institute ($206 million), the National Institute of General Medical Sciences

($121 million), and the National Institute of Allergy and Infectious Diseases ($104 million). The funding for each category by the seven leading NIH institutes is shown in table VI.2.

Table VI.2: Leading Institutes Conducting Biotechnology-Related Research, FY 1985

Dollars in millions

	Directly related		Science base		Total	
NIH institute[a]	**Cost**	**Count**	**Cost**	**Count**	**Cost**	**Count**
NCI	$206.2	(b)	$355.1	(b)	**$561.3**	**(b)**
NIGMS	120.9	1,253	161.3	1,117	**282.2**	**2,370**
NIAID	104.2	697	120.6	878	**224.8**	**1,575**
NIADDK	58.0	378	144.1	1,521	**202.1**	**1,899**
NHLBI	37.0	625	108.2	646	**145.2**	**1,271**
NINCDS	17.6	218	124.9	993	**142.4**	**1,211**
NICHD	39.8	357	83.9	677	**123.7**	**1,034**
Other	55.3	(b)	112.4	(b)	**167.8**	**(b)**
Total	**$639.0**	**(b)**	**$1,210.5**	**(b)**	**$1,849.5**	**(b)**

[a]Institute abbreviations refer, in order, to the following: National Cancer Institute; National Institute of General Medical Sciences; National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases; National Institute of Allergy and Infectious Diseases; National Heart, Lung, and Blood Institute; National Institute of Neurological and Communicative Disorders and Stroke; and National Institute of Child Health and Human Development. Except for NIAID, institutes prorate expenditures to account for only that portion of a project related to biotechnology.

[b]Not available.

Total dollars reported by the Division of Financial Management were compiled from individual institute submissions. Applying the same set of definitions, each institute develops estimates using various data bases to select biotechnology-related projects. Because of the large number of projects involved and the inconsistent way data were developed at NIH, GAO and Subcommittee staff agreed to report NIH data without examining the abstracts for conformance to NIH's definition of biotechnology.

Biotechnology Risk Assessment Research

NIH's large expenditures for the broader science effort clearly differentiate it from agencies whose mission is to provide regulatory oversight of commercial products and processes arising from biotechnology. Because it is not a regulatory agency, it does not direct its biotechnology research to risk assessments. As noted in its September 11, 1984, letter to the Subcommittee,

"Applied research aimed at directly measuring the effects on public health and the environment of release of genetically modified organisms is not generally undertaken by NIH. Information learned through basic research may form the basis for

further applied research by agencies or entities responsible for the regulation of such releases."

An NIH official in the Office of Program Planning and Evaluation told us that biotechnology risk assessment research, to the extent that it is performed by NIH, is conducted primarily at the National Institute of Environmental Health Sciences (NIEHS). NIEHS is charged with investigating the effects of chemical, physical, and biological environmental agents on human health. Therefore, we obtained abstracts of NIEHS work related to biotechnology to ascertain which contributed to risk assessment.

NIEHS classified 62 projects as biotechnology-related, including 21 research grants (of which 8 were specifically identified as directly related to biotechnology), 4 contracts, and 37 intramural projects. Of the research grants reviewed, almost all were found to include risk assessment components, but these mostly focused on chemical risks, with one aimed at radiation risks. Only 1 of the 21 grants was explicitly directed at risks that might arise from biotechnology research or production processes (but not likely from an environmental release of biotechnology products) while two others, directed at chemical risks, could possibly also be of use in assessing risks of biotechnology products.

The four research contracts included three on the same subject (the immunotoxicity of certain chemicals); the fourth was on mutagens and carcinogens. While these contracts again focus on assessment of chemical risks, one part of the immunotoxicity work (looking at resistance to various infectious agents) might, under some circumstances, be applicable to assessing biotechnology risks. Finally, of the 37 intramural research projects, only a minority had clear indications of involving risk assessment, again mostly aimed at chemical risks; and one was working on methods applicable to biotechnology risk assessment. Overall, then, of the 62 NIEHS projects whose descriptions we were given, 2 appeared to be involved in assessing biotechnology risks and 3 others, aimed at chemical risks, might also be applicable to biotechnology risk assessment.

GAO Observations

NIH described its work in this area in a letter to the Subcommittee dated May 9, 1985: "Most NIH-funded research related to biotechnology is 'research where basic issues in biotechnology are the subject' and 'biotechnology provides tools' (such as recombinant DNA or monoclonal antibodies) for the research."

We did not systematically verify NIH's classification of projects as biotechnology. However, during the process of judging NIEHS abstracts for risk assessment, we found that a large proportion of the projects at NIEHS fit under NIH's biotechnology definition.

National Science Foundation

Agencywide Research and Development

While NSF accounted for only about 7 percent of the fiscal year 1985 federal nondefense/military budget for the conduct of research and development, it is second only to NIH in support for the conduct of basic research. As shown in table VII.1, the fiscal year 1985 NSF budget provided about $1.3 billion in obligations for the conduct of research, with 94 percent of this total in support of basic research and 6 percent in applied research. NSF funds research in virtually all scientific and engineering disciplines, with particular emphasis given to the mathematics and physical sciences programs, and the astronomical, atmospheric, earth, and ocean sciences programs.

The bulk of NSF funds are distributed to colleges and universities through project grants. In addition, the Engineering Research Centers program made its first awards in fiscal year 1985 to strengthen multidiciplinary research and training in engineering at universities. Of particular relevance to this study is the fact that the area of biotechnology research was included among the first six awards made in this program. The Engineering Research Center at the Massachusetts Institute of Technology received $2.2 million in NSF funding to investigate engineering technologies for bioprocessing and perform other biotechnology-related work.

Table VII.1: Profile of NSF Research Activity, FY 1985

	Total conduct of R&D[a]	Biotechnology research	Biotechnology risk assessment
Total:			
Obligations (millions)	$1,345.6	$81.6[b]	(c)
Number of projects	14,157	1,621 to 1,773[d]	8 to 225[d]
Intramural:			
Obligations (millions)	$151.5	$0	$0
Number of projects	0	0	0
Extramural:			
Obligations (millions)	$1,194.1	$81.6[b]	(c)
Number of projects	14,157	1,621 to 1,773[d]	8 to 225[d]

[a]Total obligations were reported in OMB Special Analyses, Budget of the United States Government, 1987, Special Analysis K (Feb. 1986). The distribution of total dollars between intramural and extramural research is based on shares calculated from estimated FY 1985 data in NSF, Federal Funds for Research and Development, Fiscal Years 1984, 1985, and 1986, volume 34, table C-8. Intramural funds cover costs associated with the administration of extramural programs. The number of projects was reported by NSF.

[b]The total expenditure for the 1,773 projects that were reported to include some biotechnology related research was $126.3 million. Of that, $81.6 million was considered by NSF to be in support of biotechnology related activities.

[c]Not available.

[d]GAO estimate based on an examination of a sample of 40 out of 1,773 reported biotechnology research projects.

Definition of Biotechnology Used by NSF

NSF reported its definition of biotechnology in a letter to the Subcommittee on Oversight and Investigations, House Committee on Energy and Commerce, dated May 17, 1985, as "the application of biological systems and organisms (or parts of organisms) to technical and industrial processes." Recognizing that the broad nature of this definition has limited usefulness, NSF has further specified a category of work as "research related to biotechnology." This includes:

> "research activities in fundamental genetics, cell physiology, cell culture biology, basic biochemistry and enzymology, and bioprocess engineering, which are generally regarded as being directly related to the further development of biotechnology."

Finally, NSF uses a set of key words and phrases defining subfields and techniques that are included as biotechnology, grouped into 16 sets of terms. This list of subfields, substantially broader than the above definition, is the basis for the agency's data collection.

Biotechnology-Related Research Activity

NSF reported funding 1,773 projects that included some biotechnology-related research in fiscal year 1985. The total amount awarded for these projects was about $126 million, of which about $82 million was considered by the investigators and program officers to be directly in support of biotechnology-related activites. This biotechnology funding accounted for about 6 percent of the $1.3 billion obligated for all NSF research activities in fiscal year 1985. NSF projects related to biotechnology are found in the programs of four of the six divisions within the Directorate for Biological, Behavioral, and Social Sciences as well as in the Directorates for Engineering, Mathematical and Physical Sciences, and small amounts in Astronomical, Atmospheric, Earth and Ocean Sciences, and Scientific, Technological, and International Affairs.

In fiscal year 1985, NSF instituted a data collection system to provide detailed information on its biotechnology research support. An Office of Biotechnology Coordination was established to implement a data coding scheme that would enable NSF to identify specifically those projects related to biotechnology. The coding scheme categorizes biotechnology research into 16 fields, such as cell fusion and genetics. Program officers judge all new awards for biotechnology relatedness, assigning each project as biotechnology-related to an extent between "none" and "completely", by one-third increments. The program officer then selects up to 3 of the 16 fields to assign the project to, dividing the biotechnology portion of each project's dollars equally across as many subfields as are chosen.

Using this coding scheme, along with an expanded version of NSF's definition of research related to biotechnology, we selected a random sample of 40 projects to verify whether they were in fact biotechnology-related. All projects in the sample were found to be biotechnology-related according to NSF's broad definition. This indicates that at least 1 621 of the 1,773 NSF projects reported to us are likely to be biotechnology-related.

Biotechnology Risk Assessment Research

The GAO-selected sample of NSF biotechnology-related projects was also reviewed to determine if risk assessment activities were included in the scope of the project. We found that 2.5 percent of the sample projects included research that could be considered to contribute directly to biotechnology risk assessment. This indicates that between 8 and 225 of the projects were directly carrying out biotechnology risk assessment. An additional 75 percent of the projects provided background information that could be of value in risk assessment. The remaining 22.5 percent of

projects neither directly contributed to risk assessment nor provided background information useful for risk assessment.

In further discussions with the NSF official in charge of the agency's biotechnology research data collection, we were told that there were two small areas of research at NSF under which biotechnology risk assessment work would most likely be found: the Policy Research and Analysis and the Ethics and Values in Science and Technology programs. We found that three biotechnology-related research projects were supported under these areas in fiscal year 1985 at a combined funding level of about $250,000. One of the projects in the Ethics and Values in Science and Technology program directly involved risk assessment research, while another would probably provide background information of some use in risk assessment. The project supported by the Policy Research and Analysis Division was focused specifically on assessing risks in the application of biotechnology. In fact, it produced the document used by the new Biotechnology Science Coordinating Committee, as well as our own staff, in understanding the scope of research required for biotechnology risk assessment work.

GAO Observations

In its letter to the Subcommittee, NSF acknowledged that its definition of biotechnology, while accurate, "does not provide the specificity to define the research support activities of the agency. Under this definition of biotechnology, virtually all of the NSF supported research in biology would be considered biotechnology." In fact, looking simply at NSF's definition of biotechnology-related scientific fields (the 16 field list), we noted that this included a substantially wider scope of subjects than those included in both the "directly related to biotechnology" and the "broader science base" categories defined by NIH. In particular, large proportions of the subfields included under bioconversion, bioengineering/bioprocessing, cell regulators/mediators, chemistry, and bioenergetics, which were defined as biotechnology-related by NSF, were outside even the "broader science base" category as defined by NIH.

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